

uneventful recovery. In the interim he had had no ulcer symptoms, and he continued to drink very heavily. Twenty-four hours before the present entry bleeding began again and soon after admission the patient went into shock. The blood pressure fell to 65 mm. of mercury systolic and 40 mm. diastolic, and the pulse rate rose to 120. The condition of the patient appeared very poor despite transfusions of 500 cc. of plasma, 500 cc. of red cell mass, and 500 cc. of whole blood. After the administration of fibrin foam and the thrombin solution, there was immediate improvement and no evidence of further bleeding. The patient was discharged three weeks after admission. Results of liver function tests suggested slight liver damage. Esophagoscopy revealed no abnormality. Repeated x-ray studies showed no gastrointestinal disease until a duodenal ulcer was discovered six months after this episode.

#### COMMENT

Each of these patients was failing so rapidly that a fatal outcome seemed inevitable. The use of thrombin in gastrointestinal hemorrhage has been described by Daly,<sup>1</sup> and it was utilized in these cases as a measure of desperation. Because it was felt that there was a reasonable possibility that the bleeding might be from esophageal varices, the thrombin was given with fibrin foam in two of the cases. Three small pledgets of fibrin foam were tied to a cotton thread one inch apart. The patient was persuaded to swallow these and the thread was anchored to the cheek so that the pledgets would lie in the lower end of the esophagus. The patient was then allowed to take small sips of thrombin solution (2,500 units in 20 cc.) every two minutes. Twenty-four hours later the thread was cut and the pledgets were allowed to pass on through. In one case (Case 2) an attempt to apply this technique was unsuccessful because the patient repeatedly vomited the pledgets as well as large amounts of blood. Instead, the patient took sips of thrombin solution at two-minute intervals. Before the thrombin solution was given, Amphojel® was administered in order to buffer any free acid which might be present. The authors were unable to establish a diagnosis of esophageal varices in any of the three cases. Ultimately one patient was proved to have a duodenal ulcer.

One additional patient was treated with thrombin solution given through a Levine tube which was in place. This patient was an alcoholic who had had a gastric resection for a large ulcer on the lesser curvature of the stomach. Dilated veins made the procedure technically difficult. The liver appeared cirrhotic. Twenty-four hours after the procedure, bright red blood returned from the suction tube. In spite of conservative therapy the course was progressively downhill and thrombin was given as a supplementary measure. After irrigation of the stomach with saline solution, 30 cc. of Amphojel® and 20 cc. of thrombin solution were administered through the tube, which was then clamped off. Following this procedure, the patient improved rapidly and showed no further evidence of active bleeding. He was discharged on the fourteenth postoperative day.

#### SUMMARY

Three cases are presented in which massive upper gastrointestinal hemorrhage of undetermined cause was treated with thrombin solution either alone or in combination with fibrin foam. The favorable results suggest that the solution of thrombin may be an adjunct to conservative medical therapy.

#### REFERENCE

1. Daly, B. M.: The use of buffered thrombin in the control of upper gastrointestinal bleeding, *Arch. Surg.*, 55:208-212 (Aug.), 1947; and *J. Michigan State M. Soc.*, 46:332 (Aug.), 1947.

## Death From Metastatic Melanoma Thirty-six Years After Removal of Probable Primary Ocular Tumor

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THE appearance of long delayed metastases following enucleation of the orbit for malignant melanoma is a feature peculiar to this tumor. When confronted by a patient with a large nodular liver and an artificial eye replacing the orbit removed several years before, one should suspect a metastatic melanotic tumor to be invading the abdominal organ. Such a diagnosis was made in a patient who had generalized tumor masses 35 years after removal of the orbit. As this interval is one of the longest on record, the case is considered worthy of reporting. Another remarkable feature was that the patient had had a metastatic melanotic tumor removed nine years previously and then was free of further metastases for seven years until the present illness.

#### CASE REPORT

A 60-year-old Caucasian housewife was first admitted to the hospital February 2, 1947, complaining of left chest pain of two years' duration. Roentgenograms taken early in 1946 were said to have revealed a mass behind the heart shadow. A tumor of the left side of the neck was removed at that time. Later a slide made from a section of the tissue removed at that time was obtained. It showed that the growth removed was a metastatic melanotic tumor. The section resembled the biopsy specimen taken by the author when there was recurrence of a mass at the same site.

In 1938 a simple left mastectomy was performed because of a tumor of 18 months' duration. This tumor had gradually increased in size but was not associated with other symptoms. The hospital summary reported the findings of an obese patient with an artificial right eye and a normal chest except for the breast tumor. No axillary nodes were felt. No abdominal masses were noted. The pathologist reported that the tumor was the size of a large walnut and contained black pigment. Microscopically there was much fibrous tissue with islands of tumor cells and much pigment. No mitoses or lymph nodes were found. A diagnosis of melanoma was made.

The patient stated that in 1912, when she was 25 years of age, the right orbit had been removed about one year after the onset of progressive loss of vision. Unfortunately, a report of the findings was not available, but the patient said the eye was removed because of a deep-seated tumor, which is presumed to have been a melanoma.

The mother of the patient died at the age of 32 years with carcinoma of the breast.

Inquiry elicited no history of cough, hemoptysis or edema. There were no previous gastrointestinal symptoms or bleeding, and no genito-urinary complaints. Menopause had occurred nine years before and there had been no recurrence of bleeding.

The patient was obese, and apparently chronically ill but in no acute distress. It was evident that she had lost weight. The body surface was later carefully examined but no lesions of primary malignant disease were found. There was no evidence of recurrence of malignant growth around the right eye. The left eye was normal, as were the nose and throat. In the left supraclavicular area, a 5 by 3 cm. mass of rubbery non-tender nodes was felt. The right side of the neck was free of tumor. The mastectomy scar showed no recurrence of tumor and no axillary nodes were felt. The epitrochlear and inguinal nodes were not enlarged. The

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right breast contained no tumor. The left lower ribs were tender. There were dullness, decreased fremitus and diminished breath sounds over the base of the left lung. The heart appeared enlarged with the apical thrust in the anterior axillary line. The blood pressure was 140 mm. of mercury systolic and 70 mm. diastolic. The heart sounds and rhythm were normal. The abdomen was protuberant and soft without tenderness. A large non-tender mass in the splenic area, moving with respiration, extended downward to the level of the umbilicus. The liver edge was felt four fingers' breadth below the right costal border. It was smooth and not tender. A mass was felt in the suprapubic area. A large mass in the right buttock was felt through the rectum.

The hemoglobin content of the blood was 10 gm. per 100 cc. Leukocytes numbered from 8,500 to 11,000, with 80 per cent polymorphonuclear cells, 14 per cent lymphocytes and 6 per cent monocytes. The urine was amber colored, cloudy, acid in reaction with a specific gravity of 1.032 and a trace of albumin. The centrifuged sediment contained a few leukocytes. A chest film revealed a homogeneous density over the lower half of the left chest interpreted as probably due to tumor.

At this time, the history and reports of the eye tumor, the cervical mass and the breast tumor were not yet available so that a tentative diagnosis of metastatic carcinoma secondary to a breast malignancy seemed reasonable. Then the notation that the patient had an artificial eye, even though it had been worn for 35 years, suggested a consideration of metastatic melanoma in the differential diagnosis. With this in mind, the mass of nodes in the left neck was removed for pathologic diagnosis. At operation the nodes were seen to be deeply pigmented and the pathologist reported the tissue to be metastatic malignant melanoma.

The patient was discharged April 10, 1947, and was readmitted February 27, 1948. She had become bedridden in the interim with increased loss of weight and weakness. Examination revealed further spread and enlargement of the tumors. New growths were felt in the right side of the neck and in the left calf. The tumor in the right buttock had increased to the size of a grapefruit. The leukocyte count was 13,300 with 82 per cent polymorphonuclear cells. The urine was unchanged. It did not turn black after standing six hours. The patient died April 10, 1948. Permission for necropsy was refused.

#### DISCUSSION

Melanomas are generally considered the most malignant of all tumors because of very rapid and widespread growth once metastases appear. The spread is by lymphatic system and bloodstream, the latter being a late event and often absent until late in the course of the disease. When spread does occur, it is usually so extensive that hardly a tissue or organ escapes. For this reason, the prognosis is usually quite grave, the average duration of life being two to three years. Yet in some instances the outlook for life is not necessarily so grave as is usually stated. Following removal of an eye for a malignant melanoma, metastases, when they do occur, are said by Pack<sup>2</sup> almost invariably to lodge in the liver where they may not grow for as long as 10 to 20 years. What factors or mechanisms permit these metastatic cells in the liver or elsewhere to lie latent for this length of time are not known. They may be concerned with local tissue or organ insusceptibility or the development by the body of an environment unfavorable for the immediate multiplication and spread of neoplastic cells. Ewing<sup>1</sup> reported a case observed by Fisher and Box in which a large melanoma of the liver appeared 14 years after removal of a primary intra-ocular tumor. Ewing also cites a case reported by Albers in which local recurrence was noted 24 years after excision of a primary tumor.

Even though metastases have invaded the regional lymph nodes, removal of the primary tumor, the involved nodes, and intervening lymphatic channels may be followed by arrest of the disease. Pringle<sup>3</sup> reported on two personally followed patients who had not developed metastases 30 and 38 years, respectively, after radical resection of a cutaneous melanosarcoma and the involved regional nodes without further treatment or radiation. Wilbur and Hartman<sup>4</sup> cite a report by Wilder of a case in which the patient lived 32 years before metastases occurred.

#### SUMMARY

Twenty-six years after removal of the orbit for an intra-ocular tumor, a metastatic melanoma appeared in the breast. Seven years after a simple mastectomy, metastatic melanoma appeared elsewhere.

The interval of 36 years between removal of the primary tumor and death from metastases is one of the longest reported for delayed metastases of malignant melanoma.

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#### REFERENCES

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2. Pack, George T.: *The Biology of Melanomas*, Special Publications of the N. Y. Academy of Sciences, Vol. IV, 1948, 52-59.
3. Pringle, J. H.: Cutaneous melanoma; 2 cases alive 30 and 38 years after operation, *Lancet*, 1:508-509 (Feb. 27), 1937.
4. Wilbur, D. L., and Hartman, H. R.: Malignant melanoma with delayed metastatic growths, *Ann. Int. Med.*, 5: 201 (Aug.), 1931.

### Tetraethylammonium Chloride in Post-Herpetic Neuralgia

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THE following is a report of a case of post-herpetic neuralgia successfully treated with tetraethylammonium chloride (Etamon®). It is felt that the pronounced benefit the patient derived from the therapy warrants a trial of the drug in other cases of persistent post-herpetic neuralgia.

Beneficial results from the use of tetraethylammonium chloride in the pain of herpes zoster have been reported previously by Coller<sup>1</sup> and co-workers. Nine patients were treated. The best results were obtained in five patients whose symptoms were only of weeks' or months' duration. The other four, who had had post-herpetic pain for several years, were given a total of six to 13 intravenous or intramuscular injections each, with a total of 3,500 to 6,500 mg. tetraethylammonium chloride, spaced over seven to 17 days. Three of the four patients had only temporary relief; the fourth had 50 to 75 per cent sustained relief. No explanation could be found for the failure of the therapy in cases of long standing.

#### CASE REPORT

A 61-year-old white dishwasher entered the San Francisco Hospital complaining of severe abdominal and chest pain. He had been entirely well until August 1943 when herpes zoster developed, involving an area innervated by the seventh to eleventh thoracic nerves on the left side. The patient stated that the skin manifestations cleared promptly but that severe pain had persisted and he had to take codeine for relief of the pain. Intercostal nerve blocks kept him free of

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